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| 10/808,758 | 03/24/2004 | Daniel J. Von Seggern | 5410-006 (312552-24) | 6593 |

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| EXAMINER | |
|---|---|
| BLUMEL, BENJAMIN P | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/808,758 | SEGGERN, DANIEL J. VON | |
| | Examiner | Art Unit | |
| | BENJAMIN P. BLUMEL | 1648 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *19 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-10,14-16 and 18-48* is/are pending in the application.

4a) Of the above claim(s) *5,18-22,29-33 and 41-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,14-16,23-28 and 34-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *3/24/04* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

**DETAILED ACTION**

Applicants are informed that the rejections of the previous Office action not stated below have been withdrawn from consideration in view of the Applicant's arguments and/or amendments.

***Election/Restrictions***

This application contains claims 5, 18-22, 29-33 and 41-48, drawn to an invention and a specie nonelected with traverse in the reply filed on 7/2/08 & 11/7/08. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-4, 6-10, 14-16, 23-28 and 34-40 are examined on the merits.

***Priority***

Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/459,000 and/or the foreign priority document PCT/US03/02295 fail to provide adequate support or enablement in

the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Provisional application '000 and foreign priority document fail to teach or suggest any aspect of targeting dendritic cells or the comparison of one chimeric fiber baring adenovirus to a native fiber baring adenovirus with regard to dendritic cell interaction. Therefore, claims 1-4, 6-10, 14-16, 23, 24, 26-28 and 34-40 are only supported by the provisional application 60/467,500. As a result, the earliest priority date of the instant invention is that of May 1, 2003. In addition, the specification of the foreign priority document fails to support that limitation in claim 25 that requires that the fiber protein of Ad37 causes a reduced interaction with HSP. Therefore, the earliest priority date for claim 25 is that of provisional 60/459,000 (i.e., March 28, 2003).

***Response to Arguments***

Applicant's arguments filed 5/19/09 have been fully considered but they are not persuasive. See responses below.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 7, 9, 10, 15, 23, 24 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**(New Rejection Necessitated by Amendments)**

Claim 7 recites, "...comprising a capsid wherein the capsid includes further modifications that alter interaction with...", however, it is unclear what the "further

modifications" are since claim 7 is the first mention of a capsid and no other modified forms of a capsid are previously claimed (i.e., claims 1-6). Furthermore, it is unclear what the metes and bounds of "modification" are since numerous possibilities exist for modifying a protein (i.e., point mutations, deletions, truncations, masking, etc.). Claim 15 is rejected since it depends from claim 7.

Claims 9 and 10 recite, "...comprises at least a sufficient number of amino acids set forth as SEQ ID NO: 32 to target the particle to dendritic cells...", however, it is unclear what the metes and bounds of "at least a sufficient number of amino acids" are. Particularly since SEQ ID NO: 32 contains 365 amino acids.

Claim 23 recites, "A particle of claim 1, wherein a genome encoding the particle further comprises...", however, it is unclear if the claimed invention is the adenovirus particle of claim 1 that or a genome of an adenovirus.

**(Prior Rejection Maintained)**

Claim 28 recites, "A composition of claim 26 wherein the composition is formulated as a vaccine.", however it is unclear what this vaccine is directed towards since no additional limitations are claimed. The metes and bounds of the claims cannot be determined without further clarification.

Even though applicants have amended claim 28, the claim remains to be unclear about what is being targeted by the vaccine.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

**(New Rejection Necessitated by Amendments)** Claims 1-4, 6, 8, 14, 16, 25-27 and 34-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shankara (WO 99/47180), Dechecchi et al. (Journal of Virology, 2001) and Huang et al. (Journal of Virology, 1999).

The claimed invention is drawn to an adenovirus particle with a heterologous fiber or a portion thereof, whereby binding of the viral particle to dendritic cells is increased compared to a particle that expresses native fiber proteins. The adenovirus particle is Ad5 adenovirus (a subgroup C adenovirus) with the fiber comprising a sufficient portion from adenovirus 37 (a subgroup D adenovirus) that targets dendritic cells. The fiber can be chimeric with the N-terminus portion from a subgroup C adenovirus which is sufficient to increase incorporation into the particle in comparison to its absence in the fiber protein; or when the 15, 16 or 17 N-terminal amino acids of the Ad37 fiber are replaced with 15, 16 or 17 N-terminal amino acids of an Ad5 fiber; or the fiber is wholly from Ad37, which imparts a reduced interaction with HSP. The recombinant adenovirus particle is formulated for administration via intramuscular, IV or parenteral routes. The claimed invention also includes an adenovirus vector that encodes this recombinant adenovirus particle, which includes heterologous nucleic acids and dendritic cells that contain these nucleic acid molecules. The fiber can also be modified to reduce any interaction with heparin sulfate proteoglycans (HSP).

Shankara teaches the generation of a recombinant Ad2 (a subgroup C adenovirus) with a heterologous fiber protein or a chimeric fiber protein with heterologous portions from Ad17 (a subgroup D adenovirus). Shankara teaches that upon replacing all of the Ad2 fiber protein

except for the first 16 N-terminal amino acids with the complementing regions of Ad17 fiber proteins, dendritic cell targeting increased greater than 10 fold. (Table 2). As a result, Shankara suggests that the fiber of subgroup D adenoviruses permits the targeting of dendritic cells. Shankara also teaches the development of recombinant Adenovirus 5 with a heterologous fiber protein from Adenovirus 2. Shankara also suggests that recombinant adenoviruses can be formulated in such a way to facilitate administration via intramuscular routes. However, Shankara does not teach the use of Ad37 fiber protein segments; or the lack of HSP interaction by the recombinant adenovirus. *See pages 6, 7, 26.*

Dechecchi et al. teach the involvement of adenovirus 2 and 5 fibers for infecting cells that contain heparan sulfate glycoaminoglycans (components of HSP). Therefore, changes made to these proteins or their replacement could alter binding to HSP. *See page 8772.*

Huang et al. teach the generation of recombinant Ad37 fiber proteins for determining how amino acid mutations can alter the cellular tropism of the fiber protein. *See pages 2798 and 2799.*

It would have been obvious to one of ordinary skill in the art to modify the composition taught by Shankara in order to create a recombinant Ad5 with a fiber protein containing either all or a portion of the fiber protein from Ad37, thereby targeting dendritic cells and generating a recombinant adenovirus with a fiber protein that has a reduced interaction with HSP. One would have been motivated to do so, given the suggestion by Shankara that Ad2 (a C adenovirus) with a fiber protein from Ad17 (a D adenovirus) increases the targeting of dendritic cells. There would have been a reasonable expectation of success, given the knowledge that adenoviruses 2 and 5 use their fiber protein to interact with cellular HSP during infection, as taught by Dechecchi et

al., and also given the knowledge that mutating Ad37 fiber protein in order to determine the affect mutations have on cellular tropism, as taught by Huang et al. Furthermore, while Shankara and Huang et al. do not comment on reduced HSP interaction, this would have been a natural outcome of combining their teachings as outlined above, particularly in view of Dechecchi et al. In addition, the structure of the product is the same as is instantly claimed, thus any function(s) associated with the claimed structure is expected to be present in the structure of the prior art. Thus the invention as a whole was clearly *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

**Response to arguments:**

Applicants argue that even if one skilled in the art combined the teachings of Shankara and Huang et al., the resulting composition would not result in the claimed invention since adenovirus particles are unpredictable towards what cells they would most effectively target. Furthermore, Shankara does not mention adenovirus 37 or the HSP target and Huang et al. also fails to mention the reduction of HSP binding or the involvement of HSP binding as it relates to adenoviruses.

In response, it is acknowledged that Shankara does not mention Ad37 involvement and neither Huang et al. nor Shankara teach the interaction of adenoviruses with HSP. In addition, since Dechecchi et al. teach the interaction of adenovirus 2 and adenovirus 5 fiber proteins with HSP components on cells during infection, one skilled in the art would expect that by changing the fiber protein the HSP interaction would be affected. This is particularly the case since the fiber proteins are directly involved in cellular infection. Therefore, while Shankara does not mention mutating Adenovirus 5 by with either a fiber protein from Ad37 or a chimeric form

based on Ad5 and Ad37, the teachings of Shankara provide the methodology of making adenovirus particles with heterologous/mutant fiber proteins and also provides the motivation to create such a recombinant adenovirus which relies on a subgroup C adenovirus with a fiber protein from a subgroup D adenovirus. Therefore, the rejection is maintained for reasons of record.

***Conclusion***

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BENJAMIN P. BLUMEL whose telephone number is (571)272-4960. The examiner can normally be reached on M-F, 8-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-1600. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Stacy B Chen/
Primary Examiner, Art Unit 1648

/BENJAMIN P BLUMEL/
Examiner
Art Unit 1648